REMARKS

Claims 60-62, 67-102 and 104-112 will be pending and under consideration in the present application upon entry of the present Reply.

Claims 60, 82, 104 and 110 have been amended, and new claim 112 has been added, in order to more clearly claim the invention. The amendments are made in order to recite more clearly the invention as taught in the specification. Specifically, claim 60 has been amended to recite a method for treating a human patient in need of hematopoietic reconstitution comprising introducing into the human patient a composition comprising a cryoprotective agent and human neonatal or fetal hematopoietic stem cells derived from the umbilical cord blood or placental blood of a human collected at birth of said human so as to provide hematopoietic reconstitution. Claim 82 has amended to recite a method for treating a human patient in need of hematopoietic reconstitution comprising obtaining human neonatal or fetal blood components comprising hematopoietic stem cells derived from the umbilical cord blood or placental blood of a human collected at birth of said human; cryopreserving the blood components; thawing the blood components; and introducing the blood components into the human patient so as to provide hematopoietic reconstitution. Claim 104 has been amended to recite a method for treating a human patient in need of hematopoietic reconstitution comprising obtaining human neonatal or fetal blood components comprising hematopoietic stem and progenitor cells derived from the umbilical cord blood or placental blood of a human collected at birth of said human; cryopreserving the blood components; thawing the blood components; and introducing the blood components into the human patient so as to provide hematopoietic reconstitution. Claim 110 has been amended to recite a method for treating a human patient in need of hematopoietic reconstitution comprising introducing into the human patient a composition comprising human neonatal or fetal hematopoietic stem cells derived from the umbilical cord blood or placental blood of a human collected at birth of said human, in which the stem cells have been previously cryopreserved, so as to provide hematopoietic reconstitution.

Support for the amendments to claims 60, 82, 104 and 110 is found throughout the specification as filed, in particular at page 25, lines 19-21; page 50, lines 24-32; page 51, lines 14-23; page 66, lines 30-34; and at page 98, lines 14-15 and line 34.

Support for new claim 112 is found in the specification as filed at page 25, lines 6-7 and lines 19-21; page 47, line 9 and lines 20-23; page 50, lines 28-34; and at page 51, lines 15-16.

No new matter is added by the amendments made herein.

Rejection under 35 U.S.C. § 112, First Paragraph

Claims 60-62, 67-102 and 104-111 are rejected under 35 U.S.C. § 112, first paragraph, allegedly, because the specification, while being enabling for a method of providing hematopoietic reconstitution of a human patient comprising treating the patient to destroy the patient's endogenous hematopoietic stem cell population, and introducing into the patient a therapeutically effective amount of the human neonatal or fetal hematopoietic stem cells obtained from umbilical cord or placental blood, does not reasonably provide enablement for the method of treating a human patient as currently claimed.

Applicants respectfully disagree with the Examiner's rejection. Applicants note that claims 60, 82, 104 and 110 have been amended as described above.

In view of the Examiner's comments, Applicants respectfully submit that the Section 112, first paragraph, rejection has been overcome in view of the amendments to claims 60, 82, 104 and 110, and the remarks made below.

With regard to the Examiner's comment regarding Ende and Ende, 1972, Virginia Medical Monthly 99:276-280 ("Ende") (Reference BU, of record), that, in view of Ende, the "claims should be limited to the conditions under which engraftment occurred which requires the destruction of the endogenous stem cell population of the patient to be treated", Applicants respectfully disagree and note the following.

Regarding the "unpredictability"of engraftment, Applicants respectfully submit that the Examiner has mischaracterized Applicants' statements regarding Ende. Applicants have stated that Ende does not report achievement of hematopoietic reconstitution and provides no reasonable basis for believing that any hematopoietic reconstitution was achieved in the experiment reported by Ende[1]. The use of cord blood from multiple donors

[1] The Examiner also stated that "Applicants have not shown, and in fact emphasize in the response, that the hematopoietic stem cells of the invention engage in long term reconstitution." Applicants believe this statement represents an editorial error, and that the "not" should have been deleted, since Applicants have shown that the hematopoietic stem (continued...)

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(who have not been typed to be histocompatible), the fact that the patient was receiving anti-neoplastic compounds (6-mercaptopurine, methotrexate or vincristine, Ende at page 2, left column to page 3, left column) that kill dividing cells such as stem cells, or other reasons may account for why no hematopoietic reconstitution was achieved by Ende. Thus, one cannot conclude that the failure by Ende to destroy the immune system of the recipient is the reason why no hematopoietic reconstitution was achieved.

Further, Applicants invite the Examiner's attention to Exner et al., 1999, Ann. N Y Acad. Sci. 872:377-386 ("Exner") (Reference IX, made of record in the Second Supplemental Information Disclosure Statement submitted concurrently herewith), which discusses on page 378 results of Wood and Monaco (a 1971 reference) and McCarthy et al. (a 1985 reference) showing that total ablation of the recipient's immune system is not required for engraftment and hematopoietic reconstitution.

The Examiner's attention is also invited to Soper et al., 2001, Blood 97:1498-1504 ("Soper") (Reference IY, made of record in the Second Supplemental Information Disclosure Statement submitted concurrently herewith), which refers on page 1498, right column to results obtained by Brecher and colleagues (a 1982 reference, reference 16) that showed successful engraftment of donor cells into nonmyeloblated recipients.

Thus, Applicants submit that, contrary to the Examiner's contention, the destruction of the endogenous stem cell population of the patient to be treated is not required for successful engraftment of hematopoietic stem cells and hematopoietic reconstitution.

With regard to the Examiner's comment regarding the recitation of cryopreservative in claim 60, Applicants note that, as taught in the specification at page 47, line 34 to page 48, line 6, a cryopreservative added to the stem cells to protect the cells during freezing can be administered with the stem cells to the patient. Moreover, the Examiner's attention is invited to Kernan et al., 1994, Blood Cells 20(2-3):245-248 (Reference HB, of record), which discloses the administration of hematopoietic stem cells derived from umbilical and cord blood and a cryopreservative to a patient. Applicants note that administration of cells with cryopreservative obviates the need to remove the cryopreservative prior to administration, and thus can be desirable.

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[1] (...continued)
cells of the invention engage in long term reconstitution.

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In view of the foregoing, Applicants respectfully submit that the presently claimed invention is fully enabled and that it would not require undue experimentation to practice the claimed methods.

CONCLUSION

Applicants respectfully request that the amendments and remarks of the present response be entered and made of record in the present application. Claims 60-62, 67-102 and 104-112 fully meet all statutory requirements for patentability. Withdrawal of the Examiner's rejections and allowance and action for issuance are respectfully requested.

Applicants request that the Examiner call Adriane M. Antler at (212) 790-2247 if any questions or issues remain.

Respectfully submitted,

Date February 14, 2002

by Adriane M. Antler 32,605 (Reg. No. 40,207)
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EXHIBIT A

Serial No.: 08/442,277
Filed: May 16, 1995
Attorney Docket No.: 6287-026

MARKED-UP VERSION OF CLAIMS
UNDERLINED TEXT IS ADDED AND [BRACKETED TEXT] IS DELETED

60 (twice amended). A method for treating a human patient in need of hematopoietic [stem cell function] reconstitution comprising introducing into the human patient a composition comprising a cryoprotective agent and human neonatal or fetal hematopoietic stem cells derived from the umbilical cord blood or placental blood of a human collected at birth of said human [from the blood] so as to provide hematopoietic reconstitution [stem cell function].

82 (twice amended). A method for treating a human patient in need of hematopoietic reconstitution [stem cell function] comprising:

(a) obtaining human neonatal or fetal blood components comprising hematopoietic stem cells derived from the umbilical cord blood or placental blood of a human collected at birth of said human;

(b) cryopreserving the blood components;

(c) thawing the blood components; and

(d) introducing the blood components into the human patient so as to provide hematopoietic reconstitution [stem cell function].

104 (twice amended). A method for treating a human patient in need of hematopoietic reconstitution [stem cell function] comprising:

(a) obtaining human neonatal or fetal blood components comprising hematopoietic stem and progenitor cells derived from the umbilical cord blood or placental blood of a human collected at birth of said human;

(b) cryopreserving the blood components;

(c) thawing the blood components; and

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(d) introducing the blood components into the human patient so as to provide hematopoietic reconstitution [stem cell function].

110 (twice amended). A method for treating a human patient in need of hematopoietic reconstitution [stem cell function] comprising introducing into the human patient a composition comprising human neonatal or fetal hematopoietic stem cells derived from the umbilical cord blood or placental blood of a human collected at birth of said human [from the blood], in which the stem cells have been previously cryopreserved, so as to provide hematopoietic reconstitution [stem cell function].

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EXHIBIT B

Serial No.: 08/442,277
Filed: May 16, 1995
Attorney Docket No.: 6287-026

PENDING CLAIMS WITH AMENDMENTS MADE AS OF FEBRUARY 14, 2002

60. A method for treating a human patient in need of hematopoietic reconstitution comprising introducing into the human patient a composition comprising a cryoprotective agent and human neonatal or fetal hematopoietic stem cells derived from the umbilical cord blood or placental blood of a human collected at birth of said human so as to provide hematopoietic reconstitution.

61. The method according to claim 60 in which the composition further comprises human neonatal or fetal hematopoietic progenitor cells derived from the blood.

62. The method according to claim 60 in which the composition comprises whole neonatal or fetal blood.

67. The method according to claim 60 in which the patient has a failure or dysfunction of normal blood cell production and maturation.

68. The method according to claim 67 in which the patient has anemia.

69. The method according to claim 60 in which the patient has a hematopoietic malignancy.

70. The method according to claim 69 in which the hematopoietic malignancy is a leukemia.

71. The method according to claim 69 in which the hematopoietic malignancy is a lymphoma.

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72. The method according to claim 60 in which the patient has an autoimmune disease.

73. The method according to claim 60 in which the patient has a genetic disorder.

74. The method according to claim 60 in which the patient is immunodeficient.

75. The method according to claim 74 in which the immunodeficiency is by reason of irradiation.

76. The method according to claim 74 in which the immunodeficiency is by reason of chemotherapy.

77. The method according to claim 74 in which the immunodeficiency is by reason of infection by a pathogenic microorganism.

78. The method according to claim 74 in which the patient has a malignant solid tumor.

79. The method according to claim 60 in which the patient has Fanconi's anemia.

80. The method according to claim 60 in which the patient has a hypoproliferative stem cell disorder.

81. The method according to claim 60 in which the patient is infected by a pathogen.

82. A method for treating a human patient in need of hematopoietic reconstitution comprising:

(a) obtaining human neonatal or fetal blood components comprising hematopoietic stem cells derived from the umbilical cord blood or placental blood of a human collected at birth of said human;

(b) cryopreserving the blood components;

(c) thawing the blood components; and

(d) introducing the blood components into the human patient so as to provide hematopoietic reconstitution.

83. The method according to claim 82 in which the stem cells are autologous to the patient.

84. The method according to claim 82 in which the stem cells are syngeneic to the patient.

85. The method according to claim 82 in which the stem cells are allogeneic to the patient.

86. The method according to claim 82 in which the blood components comprise whole blood.

87. The method according to claim 82 in which the blood components are isolated by collection from an umbilical cord.

88. The method according to claim 82 in which the blood components are isolated by collection from a placenta.

89. The method according to claim 82 in which the patient is immunodeficient.

90. The method according to claim 89 in which the immunodeficiency is by reason of irradiation.

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91. The method according to claim 89 in which the immunodeficiency is by reason of chemotherapy.

92. The method according to claim 89 in which the immunodeficiency is by reason of infection by a pathogen.

93. The method according to claim 89 in which the patient has a malignant solid tumor.

94. The method according to claim 82 in which the patient has anemia.

95. The method according to claim 94 in which the patient has Fanconi's anemia.

96. The method according to claim 82 in which the patient has a hypoproliferative stem cell disorder.

97. The method according to claim 82 in which the patient has a hematopoietic malignancy.

98. The method according to claim 97 in which the hematopoietic malignancy is a leukemia.

99. The method according to claim 97 in which the hematopoietic malignancy is a lymphoma.

100. The method according to claim 82 in which the patient has an autoimmune disease.

101. The method according to claim 82 in which the patient has a hemolytic disorder.

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102. The method according to claim 82 in which the patient has a genetic disorder.

104. A method for treating a human patient in need of hematopoietic reconstitution comprising:

(a) obtaining human neonatal or fetal blood components comprising hematopoietic stem and progenitor cells derived from the umbilical cord blood or placental blood of a human collected at birth of said human;

(b) cryopreserving the blood components;

(c) thawing the blood components; and

(d) introducing the blood components into the human patient so as to provide hematopoietic reconstitution.

105. The method according to claim 104 in which the stem and progenitor cells are autologous to the host.

106. The method according to claim 104 in which the stem and progenitor cells are syngeneic to the host.

107. The method according to claim 104 in which the stem and progenitor cells are allogeneic to the host.

108. The method according to claim 107 in which the host has Fanconi's anemia.

109. The method according to claim 104 in which the blood components are isolated by collection from an umbilical cord.

110. A method for treating a human patient in need of hematopoietic reconstitution comprising introducing into the human patient a composition comprising human neonatal or fetal hematopoietic stem cells derived from the umbilical cord blood or

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placental blood of a human collected at birth of said human, in which the stem cells have been previously cryopreserved, so as to provide hematopoietic reconstitution.

111. The method according to claim 60 in which the stem cells are from the umbilical cord blood or placental blood of a single human collected at the birth of said human.

112. A method for treating a human patient in need of hematopoietic reconstitution comprising (a) thawing cryopreserved blood components comprising human neonatal or fetal hematopoietic stem cells derived from the umbilical cord blood or placental blood of a human collected at birth of said human; (b) and introducing the thawed blood components into the human patient so as to provide hematopoietic reconstitution.

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